

**WHAT IS CLAIMED IS:**

1. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:
  - 5 contacting mutant hippocampal cells having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug; subjecting said mutant cells to tetanic stimulation; and determining the effect of said <sup>candidate drug</sup> agent on the synaptic potentiation of said mutant hippocampal cells;
  - 10 wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.
- 15 2. A method according to Claim 1, wherein said mutant cells are mutated in a presenilin gene.
3. A method according to Claim 2, wherein said mutant cells are mouse hippocampal tissue slices.
- 20 4. A method according to Claim 1, wherein said enhanced synaptic potentiation is as a result of a change in the GABA<sub>A</sub> receptor pathway.
5. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:
  - 25 contacting mutant hippocampal cells, having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells, with a candidate drug; subjecting said mutant and wild-type hippocampal cells to a tetanic stimulus; measuring changes in potentiation with time of the mutant and wild-type hippocampal cells and comparing the effect of said agent on the synaptic potentiation of said mutant as compared to the observed synaptic potentiation of said wild-type hippocampal cells;
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wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells as compared to the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

- 5    6. A method according to Claim 5, including the additional steps of:  
contacting mutant hippocampal cells having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells with a GABA<sub>A</sub> receptor antagonist;  
subjecting said mutant and wild-type hippocampal cells to tetanic stimulation;  
10 and  
measuring changes in synaptic potentiation with time of the mutant and wild-type hippocampal cells and comparing the effect of said GABA<sub>A</sub> receptor antagonist on said mutant and said wild-type hippocampal cells;  
wherein a reduction in the enhanced synaptic potentiation of the mutant  
15 hippocampal cells without a <sup>statistically</sup> significant change in the synaptic potentiation of the wild-type cells is indicative of the mutation acting on a common pathway with said GABA<sub>A</sub> receptor antagonist.
7. A method according to Claim 5, wherein said agent is present with said wild-type hippocampal cells.  
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8. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:  
contacting mutant hippocampal cells having enhanced synaptic potentiation  
25 upon stimulation as compared to wild-type hippocampal cells with a candidate drug;  
subjecting said mutant and wild-type hippocampal cells to a tetanic stimulus at a first potential of glutamate currents and a second potential of GABA<sub>A</sub> currents;  
measuring the synaptic response at each of the first and second potentials for  
the mutant and wild-type hippocampal cells and comparing the effect of said agent  
30 on said mutant and said wild-type hippocampal cells;

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wherein a reduction in the enhanced synaptic response of the mutant hippocampal cells without a <sup>statistically</sup> significant change in the synaptic response of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

- 5 9. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mutant mouse hippocampal cells mutated in the presenilin-1 gene and having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells with a candidate drug;

- 10 subjecting said mutant and wild-type hippocampal cells to tetanic stimulation; and

comparing the effect of said agent on said mutant and said wild-type hippocampal cells upon tetanic stimulation;

- 15 wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a <sup>statistically</sup> significant change in the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

10. Slices of mouse hippocampal cells having a mutation in a presenilin gene  
20 combined with a candidate drug.

11. Slices of mouse hippocampal cells according to Claim 10, after tetanic stimulation.

- 25 12. Slices of mouse hippocampal cells according to Claim 10, wherein said mutation is the PS-1 Δ9 mutation.